

significant changes. We therefore agree with Chai *et al.* (1968) that as many criteria as possible need to be studied in a long-term assessment of asthmatic patients and that single, infrequent observations are of limited value.

The symptoms of house-dust allergy tend to fluctuate over the course of a year (Voorhorst *et al.*, 1967), and the possibility that the improvement in our mite-treated group could be due to this was considered. But since no similar improvement occurred in the patients in the control group over the same period it was concluded that seasonal variation was not a significant factor. Furthermore, patients who had other seasonal allergies which could confuse the results were carefully excluded from the trial. We had no information about the mite content of the house dust in the patients' homes, but no patients moved house, installed central heating, or noticeably altered their environment in any other way during the trial.

Commercial extracts of *D. pteronyssinus* for hyposensitizing treatment are unavailable. However, the more easily cultured *D. culinae* seems to have antigenic properties similar to those of *D. pteronyssinus* and it is probable that similar results would be obtained with it. Indeed, Munro-Ashman *et al.* (1970) reported successful treatment in an uncontrolled series of patients with *D. culinae* extract.

We have concluded from this trial that hyposensitizing treatment with *D. pteronyssinus* extract in patients with house-dust allergy is worth while and can offer considerable relief from their perennial asthma.

I am indebted to Dr. Kate Maunsell, who made the extracts. I thank Dr. R. S. Bruce Pearson and Dr. P. Hugh-Jones for permission to study patients under their care and for their helpful criticism. I am grateful to Miss Irene Renton for secretarial assistance and to Mr. M. Curwen, of Guy's Hospital, for help with the statistical aspects of this study.

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Metabolic Responses to Oral Glucose in the Kalahari Bushmen

B. I. JOFFE, W. P. U. JACKSON, M. E. THOMAS, M. G. TOYER, P. KELLER, B. L. PIMSTONE, R. ZAMIT

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Summary

The plasma glucose, immunoreactive insulin, and growth hormone levels after a 50-g oral glucose load have been measured in 15 adult Bushmen subjects living in the Kalahari region of Southern Africa. Compared with 10 non-obese white controls, they showed relative glucose intolerance and significantly impaired insulin secretion. Growth hormone responses showed no significant differences between the two groups. Factors such as inadequate or unusual nutrition and stress do not appear to account completely for the abnormalities in carbohydrate metabolism observed in the Bushmen. Of interest are the clinical and hormonal similarities that seem to exist between the Bushmen and the Central African Pygmies.

Introduction

The Bushmen are believed to constitute a distinct ethnic group, nowadays virtually confined to the Kalahari wastelands of Southern Africa. Physical differences from the neighbouring Negroid peoples are well described, with characteristic facial features and body build (see Fig.). They live by hunting game and collecting wild vegetation ("veldkos"), certain species of which seem to have high nutritive value (Wehmeyer *et al.*, 1969), though their dietary habits are such that periods of semi-starvation give way to episodes of overindulgence (Bronte-Stewart *et al.*, 1960).

Isolated biochemical studies in the Bushmen have shown distinctive patterns of serum proteins (Bronte-Stewart *et al.*, 1960) and lipids (Miller *et al.*, 1968), attributed to environmental rather than genetic influences, but little data exist on, potentially, one of the most intriguing metabolic aspects of all—namely, their capacity to dispose of and their hormonal response to an oral carbohydrate load. The following study was primarily undertaken in an attempt to answer this question.

Subjects and Methods

In October 1970 an expedition was made to the Dobe area in the north-western region of Botswana, where a group of !Kung Bushmen had congregated. They were all participating in the Harvard University Bushmen Project and consequently were not unaccustomed to contact with white research workers or venepuncture procedures. Fifteen apparently healthy adult members of the group were chosen for the study and a simple explanation of the intended investigation was given (by a member of the university team assisting our party). Various pertinent physical characteristics of the selected subjects are

Department of Medicine, Witwatersrand University Medical School, Johannesburg

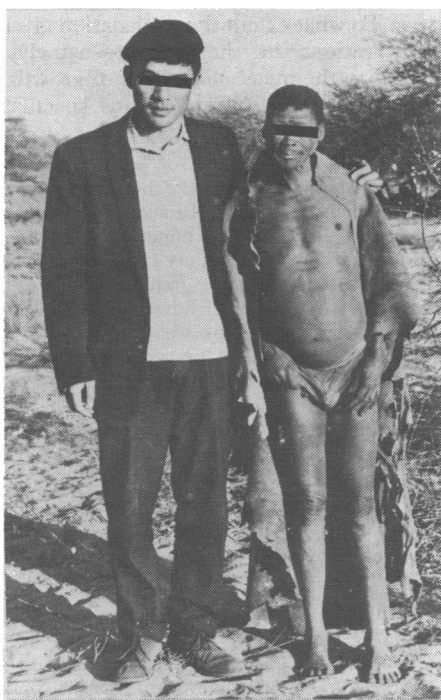
B. I. JOFFE, M.B., M.R.C.P., Research Physician
M. E. THOMAS, M.B., F.C.P.(S.A.), Medical Registrar

Endocrine Research Unit, Cape Town University Medical School, Cape Town

W. P. U. JACKSON, M.D., F.R.C.P., Director and Associate Professor of Medicine
M. G. TOYER, Senior Technician
P. KELLER, PH.D., Chief Research Officer
B. L. PIMSTONE, M.D., M.R.C.P., Senior Physician

South African Institute for Medical Research, Johannesburg

R. ZAMIT, M.B., F.F.PATH.(S.A.), Pathologist



Male Bushman standing next to a subject who is 168 cm tall.

given in Table I. Since an overnight fast would probably have been broken (owing to the almost continuous eating pattern of the Bushmen when food is available), we performed tests in the afternoon, after four hours of observed rest and fasting. At the end of this period a venous blood sample was obtained from each patient and 50 g of glucose was given by mouth. Further venous blood samples were collected at 60 and 120 minutes thereafter. During this two-hour period continued observation was maintained.

TABLE I—Pertinent Physical Characteristics (Mean and Range) of Bushmen and Control Subjects Studied

Group	No.	Age in Years*	Height (cm)	Weight (kg)	Ideal Body Weight† (%)
Bushmen:					
Males ..	8	40 (25-50)	158 (154-161)	46 (41-50)	90 (80-98)
Females ..	7	40 (15-70)	145 (138-156)	38 (27-49)	96 (76-120)
Controls ..	10	28 (18-45)	172 (155-190)	65 (42-82)	97 (88-105)

*Assessed by their physical appearance and an "events calendar."

†Adapted from Metropolitan Life Insurance Company Statistical Bulletin (1959)

The samples were placed in heparinized tubes containing aprotinin (Trasylol), immediately separated by means of a battery-operated centrifuge, and the plasma was kept in the freezing compartment of a mobile gas refrigerator. They were packed in dry ice during the flight back to Cape Town.

Plasma glucose was measured on the Autoanalyzer by the modified ferricyanide method of Hoffman (1937). Radio-

immunoassay techniques were used to determine plasma insulin (Hales and Randle, 1963) and growth hormone (Morgan and Lazarow, 1963) levels. Plasma proteins were measured electrophoretically on the fasting samples.

For comparison the plasma glucose, insulin, and growth hormone responses to a 50-g oral glucose load in 10 non-obese healthy white controls (six males and four females) aged 18 to 45 years were used. These tests were also performed in the afternoon, after a four-hour fast, to obviate any discrepancies that might have arisen because of the diurnal variation in oral glucose tolerance (Jarrett and Keen, 1970).

Results

The results of the plasma glucose and insulin responses in the 15 Bushmen and 10 control subjects after oral glucose are summarized in Table II. Mean glucose levels were higher in the Bushmen at all stages, with significant differences at 0 and 120 minutes. Indeed, by lax criteria of evaluation (Jackson *et al.*, 1970), their mean two-hour post-glucose level of 121 mg/100 ml could be regarded as falling within the "diabetic" range. Conversely, the Bushmen exhibited insulinopenia throughout the test, and this was significant at 0 and 60 minutes. Calculation of the "insulinogenic" indices for the two groups served to accentuate the impaired insulin production occurring in the Bushmen. There was no significant differences in glucose or insulin values between the male and female Bushmen subgroups.

Growth hormone responses are outlined in Table III. Fasting plasma growth hormone levels showed no significant difference between the Bushmen and control subjects, and in both instances there was prompt suppression to near zero concentrations after glucose administration.

TABLE III—Mean (\pm S.E. of Mean) Growth Hormone Responses in the Bushmen and Control Groups during Glucose Tolerance Test

Group	No.	Plasma Growth Hormone (ng/ml)		
		0 min	60 min	120 min
Bushmen	15	2.0 (\pm 0.5)	0.8 (\pm 0.2)	0.9 (\pm 0.3)
Controls	10	3.9 (\pm 1.3)	0.9 (\pm 0.2)	1.3 (\pm 1.3)

Finally, measurement of plasma proteins in the fasting samples of the Bushmen gave a mean total value of 7.6 (\pm 0.3) g/100 ml, with a mean albumin fraction of 3.7 (\pm 0.2) g/100 ml. Corresponding values in the controls were 6.3 (\pm 0.3) and 4.1 (\pm 0.4) g/100 ml.

Discussion

In the light of observations suggesting an inverse correlation between the degree of sophistication of population groups and their ability to metabolize effectively an oral glucose load (Rubenstein *et al.*, 1969; Jackson, 1970), the relative carbohydrate intolerance of our primitive Bushmen subjects is at first glance rather surprising. Since it was impossible to ensure

TABLE II—Mean (\pm S.E. of Mean) Plasma Glucose and Insulin Responses of Bushmen and Control Subjects during 50-g Oral Glucose Tolerance Test

Group	No.	Plasma Glucose (mg/100 ml)			Plasma Insulin (μ U/ml)			Insulinogenic Index Insulin Δ Glucose Δ
		0 min	60 min	120 min	0 min	60 min	120 min	
Bushmen	15	95 (\pm 2)	169 (\pm 11)	121 (\pm 7)	10 (\pm 1)	33 (\pm 5)	20 (\pm 3)	0.17
Controls	10	85 (\pm 2)	142 (\pm 7)	101 (\pm 6)	15 (\pm 1)	63 (\pm 9)	30 (\pm 5)	0.35
Significance	P < 0.05	N.S.	P < 0.05	P < 0.01	P < 0.01	N.S.	P < 0.001

Δ = Calculated area under tolerance curve.

an adequate carbohydrate intake among the Bushmen for some days before testing (nor did we want to alter their usual dietary habits) we were initially tempted to attribute the findings to a form of "starvation diabetes." However, several features mitigated against this possibility: a retrospective dietary history (M. J. Konner, personal communication, 1971) indicated that the Bushmen, in fact, consumed fairly large amounts of carbohydrate-rich vegetable food during the week before testing; their mean fasting plasma glucose level was raised rather than low; their pattern of insulin secretion was not sluggish and persistent (Tzagournis and Skillman, 1970); nor did their mean plasma albumin level suggest severe protein undernutrition.

Was the unusual diet of the Bushmen per se responsible for their impaired glucose tolerance and subnormal insulin release? Consumption of large amounts of mannoheptulose (occurring most abundantly in the avocado), for example, will block insulin release, with resultant hyperglycaemia (*Nutrition Reviews*, 1971), but no information is available concerning its content in Bushmen "veldkos."

A pronounced stress reaction at the time of the investigation could have produced a similar metabolic pattern (Jackson *et al.*, 1970), but as none of the primitive subjects became overtly distressed during the test—a fact supported by their normal fasting growth hormone levels—this, too, seemed an unlikely explanation. Consideration was also given to the hypothesis that the significant impairment of insulin secretion reflected a degree of beta cell failure (or adaptation) induced by a variety of unfavourable environmental (and/or genetic) factors to which the Bushmen have been exposed.

Finally, the apparent similarity between certain of our results and those reported in the Central African pygmies by Merimee *et al.* (1968, 1969) and Rimoin *et al.* (1969) are of interest. Not only is the average height and weight of the two groups comparable but the pygmies also manifest abnormal glucose tolerance curves in some instances, significant post-glucose insulinopenia, and normal, suppressable, basal growth

hormone levels. To what extent the explanation given to account for these observations in the pygmy—namely, end-organ unresponsiveness to the metabolic effects of growth hormone—can be applied to the Bushmen, remains speculative for the moment.

It is a pleasure to acknowledge the help given by members of the Harvard University Kalahari Project, especially Professor I. DeVore and Mr. and Mrs. M. J. Konner. The chemical pathology department of Cape Town University Medical School performed the protein determinations. We are grateful to Drs. Trefor Jenkins and H. C. Seftel for their helpful advice and criticisms. Valuable help in preparing the manuscript was provided by Mrs. R. E. Joffe and the Witwatersrand University Medical Photography Unit. The study was financed, in part, by the South African Medical Research Council.

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PRELIMINARY COMMUNICATIONS

Nephrotic Syndrome in Monkey Infected with Human Quartan Malaria

A. VOLLER, C. C. DRAPER, TIN SHWE, M. S. R. HUTT

British Medical Journal, 1971, **4**, 208–210

Summary

A splenectomized aotus monkey infected with human quartan malaria (*Plasmodium malariae*) developed oedema and proteinuria. Histological examination revealed a generalized diffuse glomerulonephritis and immunofluorescent staining showed granular deposits of IgM in the glomeruli. The

pathological picture resembled that shown by human patients with the quartan malaria nephrotic syndrome.

Introduction

The association between *Plasmodium malariae* infection and the nephrotic syndrome has now been convincingly demonstrated in several areas of Africa (Gilles and Hendrickse, 1963; Kibukamusoke, Hutt, and Wilks, 1967), and the suggestion of Hendrickse and Gilles (1963) that the pathological picture might be the result of damage to the kidney by immune complexes has been shown to be correct as recent immunofluorescent observations (Allison *et al.*, 1969; Ward and Kibukamusoke, 1969; Houba, Allison, Adeniyi, and Houba, 1971) have shown the presence of complexes in the kidneys of affected children.

Experimental work in the past has been hampered by the absence of a suitable animal model, and it is only recently that *P. malariae* has been adapted to a convenient primate, *Aotus trivirgatus* (Geiman and Siddiqui, 1969). The present communication describes the development of nephrotic syndrome in an aotus monkey infected with *P. malariae*.

Materials and Methods

The strain of *Plasmodium malariae* of human origin was obtained from Dr. R. Ward, of the Walter Reed Army Institute

Nuffield Institute of Comparative Medicine, the Zoological Society of London, London N.W.1

A. VOLLER, D.Sc., Senior Lecturer

London School of Hygiene and Tropical Medicine, London W.C.1

C. C. DRAPER, D.M., D.P.H., Senior Lecturer

TIN SHWE, M.B., B.S., D.C.M.T., Research Assistant

St. Thomas's Hospital Medical School, London S.E.1

M. S. R. HUTT, M.D., F.R.C.P., Professor of Geographic Pathology